December 2023

Toxic Adulterant Alert: Medetomidine/Dexmedetomidine

This alert is to warn substance abuse treatment providers, clinicians, public health agencies and testing labs that medetomidine/dexmedetomidine has been identified as an adulterant in illicit drug materials. It belongs to the same drug class as the adulterant xylazine, a veterinary tranquilizer, and has /similar adverse effects including bradycardia, hypotension, and CNS depression, however, medetomidine is considered more potent.

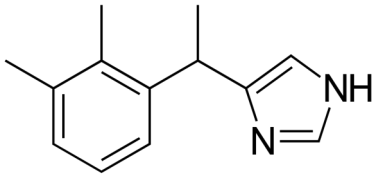
Medetomidine (Domitor®) has recently been identified as an adulterant in illicit drug material. Since July 2022, it has been detected in several seized drug samples across the state of Maryland, and in drug paraphernalia and illicit drug seizures submitted to public health and law enforcement agencies. It was most frequently observed in samples containing fentanyl and xylazine, though medetomidine has also been identified together with fentanyl analogs, heroin, and cocaine. Medetomidine has also been detected in overdoses in St. Louis and clandestine laboratory seizures in Ohio, Florida, and Canada. It is typically a minor component in the these samples, but is of toxicological concern.

Background:

Medetomidine is a potent surgical anesthetic approved for veterinary use in both large and small animals. Another form of the drug, its dextro-isomer dexmedetomidine (Dexdor®, Precedex®) is also utilized in human medicine. Clinically, it is used to induce sedation, analgesia, anxiolysis, and muscle relaxation in both humans and animals. The compound belongs to the class of α2-adrenoceptor agonists, which also includes xylazine, romifidine, and detomidine. Veterinary studies have shown medetomidine to be a more potent, selective, and specific agonist in the peripheral and central nervous systems than xylazine.

To date, reports involving human poisonings with medetomidine/dexmedetomidine are rare. An unintentional poisoning involving medetomidine and a related compound, detomidine, of a farmer working with livestock has been reported. The farmer experienced significant drowsiness, dizziness, CNS relaxation, bradycardia, and hypotension before making a full recovery. A three year old child accidentally administered 100ug of dexmedetomidine had bradycardia and reduced respiration and was unconscious for seven hours, before recovering.

Medetomidine



Recommendations for Clinicians

- Be aware that illicit drugs may contain **medetomidine** which can complicate the clinical presentation.
- Be familiar with the signs and symptoms associated with **medetomidine** intoxication.
- Be aware that most hospital-based clinical laboratories do not offer **medetomidine** toxicology testing.

Indicators of Toxicity

- Sedation
- Analgesia
- Dry mouth
- Respiratory depression
- Hypnotic/anesthetic effects
- Mydriasis
- Hypothermia
- Spontaneous muscle contractions (twitching)
- Bradycardia
- Initial hypertension, followed by prolonged hypotension

Recommendations for MEs & Coroners

- Test for common adulterating agents in suspected opioid– or fentanyl– related death cases where medetomidine may be present.

Recommendations for Forensic and Clinical Laboratories

- Consider monitoring for **medetomidine** during routine testing.
- Develop sensitive confirmatory procedures for common adulterating agents, including **medetomidine.**
- Consider laboratory analysis of seized drug samples taken from suspected drug overdose. investigations.
- Share data on adulterants in drug seizures in your jurisdiction with local health departments, medical examiners, and coroners.
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Health Impacts:

Medetomidine has been identified as a component in illicit drug samples.

Commonly known side effects of medetomidine include dose-dependent sedation, analgesia, anxiolysis, and muscle relaxation.

While dexmedetomidine is used frequently in human medicine, reports on medetomidine administration in humans is limited but demonstrates an α2-agonistic mechanism of action. In general, medetomidine studies in humans have shown dose-dependent hypotension and bradycardia. Both subjective and objective sedative effects have been observed after single intravenous doses, including sedation noted after a dose of 25 mcg. Medetomidine also reduces norepinephrine and increases human growth hormone levels in plasma.

Animal studies have shown the following adverse effects:

> ***Cardiovascular effects:*** Initial, short-lived hypertension followed by dose-dependent hypotension and bradycardia.
> Increased chance of arrythmias.
> ***Respiratory effects:*** Decreased respiratory rates and overall respiratory depression.
> At high doses, hypnotic or anesthetic effects as well as spontaneous muscle contractions can occur.
> Induces dose-dependent mydriasis.

Medetomidine-induced sedative effects can be inhibited in animals with α2- adrenoceptor antagonists, including atipamezole and yohimbine, however this has not been formally evaluated in humans.

The adverse symptoms of medetomidine/dexmedetomidine over-exposure should be treated with supportive respiratory care and management of blood pressure. Medetomidine does not respond to naloxone (Narcan®). However, naloxone administration is recommended inillicit drug exposure because medetomidine is almost always found in combination with opioids.

Similar to warnings with xylazine, concomitant use of medetomidine with cocaine, opioids, or a combination may potentiate or prolong the effects of these drugs, which can lead to adverse consequences.

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